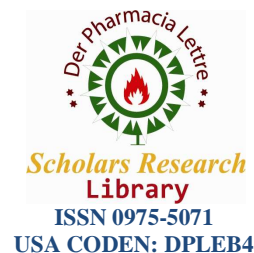




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A Review study of chemical constituents and Side-effects of black henna for children

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ABSTRACT

Henna (*Lawsonia inermis*) belongs to Lythraceae family is widely used in Islamic and Hindu cultures to dye their skin, hair, and nails. There are three different kinds of Henna: red henna, neutral henna and black henna. Red henna dye the skin reddish-brown, neutral henna dye no color while Black henna (the combination of red henna with p-phenylenediamine (PPD)) is used for temporary 'black henna tattoos'. This article provides a full review of the side-effects of topical application of red and black henna, both cutaneous (allergic and non-allergic) and systemic on children. This review article was carried out by searching studies in PubMed, Medline, Web of Science, and Iran Medex databases up to 2015. totally, of 156 found articles, 64 articles were included. The search terms were "black henna", "side-effects", "children", "Lawsonia", "p-phenylenediamine". In children with glucose-6-phosphate dehydrogenase deficiency, topical application of henna may cause life-threatening hemolysis. Black henna tattoos will induce contact allergy to its ingredient PPD at an estimated frequency of 2.5%. Once sensitized, the patients may experience allergic contact dermatitis from the use of hair dyes containing PPD. Topical application of black henna was shown to trigger allergic, non-allergic and systemic side-effects including hemolysis, localized hypertrichosis, allergic contact dermatitis i.e. depigmented spots, itching, erythema, enduration, Erythematous, residual hypopigmentation, intense facial and scalp dermatitis in children. The sensitization of children to PPD may have important aftermath for their health and future life. Thus, its topical application should be forbidden by authorities.

Key words: black henna, side-effects, children, Lawsonia, p-phenylenediamine

INTRODUCTION

Lawsonia inermis is a single-species genus of the Lythraceae family, its leaves, stem bark, roots, flowers and seeds have been used in traditional medicine. It was used to dye skin, hairs and fingernails and body [1, 2]. it is a shrub grown in India, Sri Lanka, and North Africa; it is applied topically while mixed with other substances [3, 4]. There are three types of henna like Neutral henna, Red henna and Black henna. Neutral henna, a green powder that smells like freshly cut grass, is neither henna nor neutral. Neutral henna or *Cassia obovata* does not stain hair. Red henna, a green powder that smells like hay. The leaves of the henna plant possess a red-orange stain molecule: lawsone, a naphthaquinone compound. Henna cause to dye your hair reddish; but this stain is translucent and will combine with your natural color. Black henna, a green powder that smells like frozen peas, is neither black nor henna. It is indigo, *Indigofera tinctoria*. Black henna is the combination of red henna and the dye PPD. When henna is a small and immature plant, it has low dye content and is spineless; when mature, it develops spines and higher dye content [5].

Black henna [or blue henna] is the combination of red henna and PPD. There is no natural black henna. Some of these 'henna' preparations do not even contain red henna at all [6, 7]. PPD is added to henna to fast the dyeing and drying process, to strengthen and darken the color, to improve the design pattern of the tattoo, and to cause the tattoo last longer. These tattoos stain the skin black, and look like a real tattoo. Because mixtures of black henna tattoo are often prepared by the artist with a variety of materials and sources, the actual concentrations of PPD and other ingredients is likely to be quite varied. Black henna can be distinguished from red henna in that it is dark brown or black, does not change color when moistened, and is fixed on the skin in less than one hour while, pure red henna is green-grey in color, stain orange when moistened, and last between 2 and 12 hours to be fixed on the skin [6].

While henna has lots of therapeutic effects like antimicrobial, antioxidant, anticancer and antiparasitic activity [8, 9], skin cancer chemo preventive activity [10], joint pain treatment, ulcers and wound treatment, treatment of liver and digestive disorders, reduction of tissue loss in leprosy, diabetic foot disorders and ulcers [9], diabetes mellitus treatment [11]. It was reported to have anti-inflammatory effect [12], it has lots of side effects. To make the hair and eyelashes colored by henna, one should be careful because there is a risk of damaging the eye [13]. Henna can cause skin irritation and contact dermatitis [Red henna was reported to be generally safe [14, 15]. Henna leaves cause infertility in mice. Its leaves have narcotic effect and high levels of it can cause headaches and intoxication [16]. henna tattoo patterns on both forearms and hands may hurt peripheral venous cannulation [17]. *L. inermis* may have teratogenicity and should be used cautiously during pregnancy [18]. It also cause hemolytic anemia in G6PD-deficient patients [19, 20], cause to slow heart rate with increasing the scope of its contract.

Temporary henna tattoos have become very fashionable as a safe substitute to permanent tattoos [skin painting or pseudo-tattooing] in America, Spain, Canary islands, France, and Greece, Turkey, Egypt, the United States [Hawaii, Florida, and California], Mexico, Australia, South-east Asia [Indonesia, Thailand, India, and the Philippines], and South Africa among children and adolescents, especially at festivals. Black henna is available in market as either do-it-yourself kits [21, 22] or ready-to-use henna paste, or are made by patients themselves [23, 24]. At Present, temporary henna tattoos contain not only henna, but also other additives such as para-phenylenediamine [PPD], which is considered to be the chemical agent that most frequently causes skin reactions associated with the use of commercial black henna. PPD cause extreme sensitization, and often exists in the tattoo at high concentrations [25]. Application of the tattoo and the first signs of dermatitis were usually between 8 and 14 days, but, in many cases of active sensitization, short incubation periods of 4–7 days have been seen, especially in children. This is attributed to the PPD strong sensitizing activity [26, 27].

Since 1997, black henna tattoos have been largely reported as a cause of allergic skin reactions. Most patients have been children, adolescents, or young adults. Most patients with an allergic reaction become sensitized to PPD in the tattoo itself. Causes of reaction were mostly reported to be de novo sensitization from the tattoo, allergic contact dermatitis in black henna tattoos in patients already sensitized to PPD, and allergic reactions to products containing PPD or related compounds, such as hair dyes, in patients probably previously sensitized by black henna tattoo. In a study in UK, it was shown that 7% of adult and 14% of their children had a temporary tattoo [28]. Paraphenylenediamine toxicities are reported usually after its ingestion; however, there are some cases of systemic toxicity after its local application as hair dye [29, 30]. Para-phenylenediamine [PPD] in black henna tattoo mixes is widely recognized as a cause of type-IV allergic contact dermatitis. Legislation in Western countries prohibits the use of PPD on the skin and limits the use in hair dye [21]. It often takes several weeks for the dermatitis to relieve, despite topical and sometimes oral corticosteroid therapy. Long-lasting pigment alterations are observed frequently.

Chemical compound

The plant is reported to contain quinones, phenyl propanoids, flavonoids, terpenoids, phenolic compounds and fatty acids [31], carbohydrates, glycosides, tannins, phenolic compounds and gums and mucilage. Its leaf was illustrated to contain total ash, acid insoluble ash, and water soluble ash. The percent practical yields of alcohol and aqueous extract percent yield were found to be 12.34 % and 15.50 %. Alcoholic and aqueous extracts were shown to have carbohydrate, glycosides, tannins, phenolic compounds and gums and mucilage. none of the following substances were observed in this plant i.e. saponins, alkaloids, phytosterols, fixed oils, fats, proteins, amino acids, volatile oils [5]. Its anti-diarrheal effect is due to Tonus reduction and mass movement (peristalsis) of colon. Its Anti-inflammatory, analgesic and anti-fever effects, Antibacterial and antifungal effect has been reported to the existence of Lawsonia [16]. (1).p araphenylenediamine (PPD) that is an alanine derivative, which is added as a strong oxidizer and dyeing accelerator to henna powder, is the major element of black henna. heavy metals were found in black henna including cobalt, mercury, nickel, chromium, lead, silver nitrate, iron oxide, and titanium dioxide, pyrogallol

and substances such as ethyl cellulose and tartaric acid may be added to black henna(32). In 12 commercial and traditional henna samples, lead was found at concentrations in some types of black henna paste (33). Nickel and cobalt were identified in some henna samples available in Taiwan, but at very low concentrations (34). In the great majority of black henna products, it is PPD that is added, but sometimes m-phenylenediamine or o-phenylenediamine are added(35).

Mechanism of action

generally, dying and pharmacological properties of henna are due to the existence of a substance called Lawsonia, but this substance does not act alone, and especially its coloring properties depends on other substances(1). A large number of aromatic compounds were found in many hennas, both 'natural' and 'commercial'(36). The samples with higher concentrations of these aminophenols always contained high concentrations of PPD and/or m-phenylenediamine, so it may be more likely that they are either impurities or chemical reaction products. The same goes for p-nitroaniline and aniline, both of which are unlikely to have been actually added. The structure and redox potential of lawsone (2-hydroxy-1, 4-naphthoquinone) are similar to those of 1,4-naphthoquinone, a metabolite of naphthalene and a potent oxidant of glucose-6-phosphate dehydrogenase (G6PD)-deficient cells(37).

Side-effects of black Henna on children

Side effects of henna were divided into three types: Allergic side-effects of black henna tattoos, Non-allergic side-effects of black henna tattoos and systemic side effects.

Allergic side-effects of black henna tattoos

An 11-year-old boy applied a black henna tattoo. After 3 days he developed an itching rash at the site of the tattoo that spread to the rest of the body. high dose of PPD in the black henna This was most likely caused an allergic contact dermatitis and erythema exsudativum(44). An 11-year-old boy who got a temporary black henna tattoo on his right arm during the summer holidays in Greece and developed a severe contact dermatitis at the tattoo site with residual hypopigmentation. No record of contact dermatitis was seen but the child suffered from seasonal allergic rhinitis and atopic dermatitis. a strong reaction to PPD was observed in patch test(45, 46). In another study, the use of temporary henna tattoos in children be discouraged(47). A 7-year-old boy who reported erythematous popular bull's-eye shaped lesions and consolidated edema in the upper and lower extremities was referred to hospital. He also showed an erythematous-eczematous lesion on his leg, shaped like a dolphin. In this area, a temporary henna tattoo was dyed 1-month earlier. Patch test was positive for paraphenylenediamine (PPD)(48).

A 13-year old boy who suffered from itching, erythema, enduration on the application site, increasingly urticarial rash, conjunctivitis and swelling of the lips 48 h after being applied the temporary henna tattoo was hospitalized. He had a local reaction to henna tattoo when he was 5-year old. He was treated with parenteral corticosteroids and oral antihistaminic drugs. Skin reactions persisted for 18 days. The patient showed no early reaction to henna 10% and PPD 1% concentration in saline solution but did late reaction (after 48 h) to PPD in diameter of 12x13 mm in prick test in 3 weeks after the reaction. A case who developed angioneurotic edema and urticaria to temporary henna tattoo was also observed(49).

3 children of the same age who applied henna to their hair, developed a severe contact dermatitis with massive face and neck swelling. All 3 cases had a previous history of mild local reactions to henna. Their reactions are continued to be due to sensitization to para-phenylenediamine. This reaction could result in permanent skin changes(50). a 6 year-old patient was observed with a black henna tattoo on his right leg was diagnosed with contact dermatitis .the patch test was shown that it was due to PPD(51).

Two brothers aged five and eight years with classical sensitization and illustrative contact dermatitis after repeatedly exposure to black henna were presented. The patch testing was positive for hyper-sensitivity reaction to PPD. The case serves as a reminder on the potential consequences of a harmless skin drawing(52). Two cases of allergic contact dermatitis due to temporary tattoos in children were observed. In one case, a patch test was positive for PPD(53). a case of angioedema-like allergic contact dermatitis related to hair coloring with henna in children(54). Dyeing hair with black henna resulted in allergic contact dermatitis of the scalp and face, with upper airway obstruction, in a 15-year-old girl; patch tests were not performed(55). Six children with severe allergic reactions to hair dyes after sensitization to black henna tattoos were diagnosed within 2 years (2003 and 2004) in two hospital clinics that, on a yearly basis, 5% of the suspected contact dermatitis patients in Denmark(56). Another 6 patients with hair dye allergy after sensitization by black henna tattoos were seen over a 2-year-period in one

hospital in Toronto, Canada (57). Once sensitized, the patients may experience allergic contact dermatitis from the use of hair dyes containing PPD or related chemicals. Such reactions are often fierce, especially in children, and many of them required to be hospitalized. Besides, many of those sensitized to PPD have cross-reactions to other hair dyes, dyes used in textiles, local anesthetics, and rubber chemicals, contact with which needs to be avoided (58).

Non-allergic side-effects of black henna tattoos

There have been some reports of the appearance of localized hypertrichosis after black henna tattoos without allergic reactions to the tattoo (59, 60). One case of cutaneous mercury deposition after the application of henna dye containing red pigment with a painful cutaneous granuloma and abscess in a 13-year-old has been presented; the subcutaneous tissue with the mercury materials had to be removed surgically (61). In an 8-year-old girl from India, depigmented spots at the tattoo site were seen 3 days after its application. Prior to this, the tattoo had been partially removed because of extreme itching, but no dermatitis developed. The depigmentation was ascribed to PPD; patch tests were not performed (62).

Systemic side-effects

The primary symptoms of toxicity from body painting are massive edema of the face, lips, glottis, pharynx, neck, and bronchi, occurring within hours of application of the dye mix to the skin, and sometimes requiring emergency tracheostomy for respiratory obstruction. Ingestion of the mix or PPD alone, either accidentally (in children), deliberate (suicidal), or homicidal, leads to similar clinical presentations with, additionally, rhabdomyolysis. Many patients die within 24 hours (63, 64). The cumulative effects of prolonged lead exposure may be of concern, especially in children (33). Topical application of henna may trigger severe hemolysis in children with G6PD deficiency. Signs and symptoms may include pallor, lethargy, vomiting, jaundice, anemia, tachycardia, poor peripheral perfusion, shock, and even mortality (37-43).

CONCLUSION

The sensitization of children to PPD may have important aftermath for their health and future life. Thus, its topical application should be forbidden by authorities.

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